

## REMARKS

Applicants acknowledge receipt of an Office Action dated June 13, 2008.  
Reconsideration of the present application is respectfully requested.

### I. Status of the Claims

Claims 5-25, 69, 97-107 and 115-122 were not subject to the original restriction requirement because they recited an improper multiple dependency. This status is corrected presently by amendments to withdrawn claims 5, 6, 9-11, 21-23, 97-98, 101, 103, 104, 106, 115, 117, 119 and 121, and to claim 96, which was not withdrawn. Claims 25, 107 and 122 have been cancelled without prejudice or disclaimer. Applicants respectfully request rejoinder and examination of claims 5-24, 69, 97-106 and 115-121.

The remaining non-elected claims 26-93 have been cancelled without prejudice or disclaimer.

Claim 114 is cancelled, without prejudice or disclaimer. The subject matter of claim 114 is incorporated by amendment into claims 1, 94, and 108. These amendments are supported by claim 114 and the translated specification at, *e.g.* p. 19, ll. 10-11; p. 21, l. 28 to p. 22, l. 3; p. 23, ll. 26-28; p. 42, l. 20 to p. 43, l. 8; Example 37 (p. 104, l. 4 to p. 105, l. 10); original claims 64, 97, 114; and Figures 31-33.

A minor typographical error has been corrected in the chemical structure displayed in claims 2, 94 and 108.

Claim 97 is amended in view of the incorporation into claim 94 of the subject matter of claim 114.

Claims 17-20 have been amended to clarify that the N-linked glycosylation is on the mammalian protein being expressed in the methylotrophic yeast strain.

Claims 100, 103, 105, 116, 118 and 120 depended from claim 83, which depended from claims 80-82. Claims 80-83 are cancelled. The subject matter of cancelled claims 80-83 is incorporated into claims 100, 103, 105, 116, 118 and 120.

Claims 1, 94 and 108 have been amended to replace “which is capable of producing” with “which produces.”

The foregoing amendments are made without prejudice or disclaimer, and do not introduce new matter. Entry and consideration of the amendments is requested.

Following entry of these amendments, claims 1-24, 94-106, 108-113, and 115-121 are pending, and claims 1-4, 94-96 and 108-113 are under examination.

## **II. Information Disclosure Statement**

The documents listed on the Information Disclosure Statement filed 8/16/05 are electronically resubmitted with this reply.

## **III. Rejections Under 35 U.S.C. § 102(b)**

Claims 1-3 were allegedly anticipated by WO 02/00856 to Contreras *et al.* (“Contreras”). Recitations from claim 114, which was not rejected over Contreras, are incorporated into claims 1-3. The rejection is overcome, therefore, and its withdrawal is therefore requested.

## **IV. Rejections Under 35 U.S.C. § 103(a)**

Claims 4, 94-96, and 108-113 were rejected as allegedly obvious over Contreras in view of U.S. Patent Publication No. 2007/0077642 (“Strauss”). As noted above, however, the relevant base claim(s) are revised to incorporate the salient recitations of claim 114, which was not subject to this rejection.

It necessarily follows that the cited combination, which does not teach or suggest all elements recited in the claim at issue, does not validate a *prima facie* case under Section 103. For this reason, at least, the rejection cannot stand and should be withdrawn.

Applicants would add that the specification also underscores certain aspects of their claimed invention that the prior art does not presage. Thus, part of the antibody heavy chain was degraded when antibody heavy and light chains were expressed in *Ogataea minuta* OCHI knockout mutant TK9-IgB-aM (och1Δ pep4Δ prb1Δ ura3Δ ade1Δ). See Example 28, particularly at page 93, lines 19-21. Knockout of the YPS1 gene prevented degradation of the

heavy chain, as demonstrated by expression in *Ogataea minuta* YK2-IgB-aM strain (och1 $\Delta$  pep4 $\Delta$  prbl $\Delta$  ura3 $\Delta$  ade1 $\Delta$  yps1 $\Delta$ ). See Example 38, especially page 106, lines 6-17. Accordingly, the knocking out of both OCH1 and YPS1 genes, with the addition of an  $\alpha$ -1,2-mannosidase gene, produces a strain that can produce a full-length antibody molecule, comprised of two heavy chains and two light chains, that is glycosylated with Man<sub>5</sub>GlcAc<sub>2</sub>.

**V. Rejections Under 35 U.S.C. § 112, First Paragraph**

At page 4, claims 95, 96, and 109-113 were rejected on grounds that prompted Examiner Vogel to suggest the submission of a declaration, attesting to a deposit of recited yeast strain IFO 10746, in accordance with 37 C.F.R. 1.801 through 1.809. Since such a declaration accompanies this response, withdrawal of the rejection is warranted.

**VI. Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-4, 94-98, and 108-113 stand rejected for alleged indefiniteness in the recitation of “capable of” in claims 1, 94, and 108. Page 6 of the Office Action states that “this phrase refers to a latent ability; it is unknown whether the ability is expressed or observed in the invention.”

Applicants submit that this rationale does not stand up to reasoned scrutiny. Examples 24, 27-29, 38 and 39 demonstrate that yeast strains having disrupted OCH1 gene and expressing  $\alpha$ -1,2-mannosidase produce glycoproteins with a mammalian type, high mannose type sugar chain. Still, the ability to produce a mammalian type sugar chain may be latent if the genes responsible for this property are under the control of an inducible promoter (e.g., *AOXI*): such strains are therefore “capable of” but may not be presently producing “a mammalian type sugar chain.”

In the context of the present invention, as elaborated in Applicants’ specification, the skilled person therefore would not consider “capable of” to be unclear. Nevertheless, since the contested phrase, appearing the claim preamble, holds no significance for claims scope, applicants are willing to advance prosecution by replacing “which is capable of producing” with “which produces.” The stated grounds for rejection are inapposite to the present claims, therefore, and withdrawal of the rejection is requested.

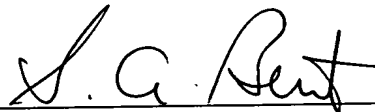
**CONCLUSION**

Applicants submit that the pending claims are in condition for allowance, and they request an early notice to this effect. Examiner Vogel is invited to contact the undersigned directly, should she feel that any issue warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 C.F.R. §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then Commissioner is authorized to charge the unpaid amount to the same account. If any extension is needed for timely acceptance of submitted papers, then Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of the relevant fee(s) from the account.

Respectfully submitted,

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